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Colourimetric-based method for the diagnosis of spinal muscular atrophy using gold nanoprobes

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Abstract: Although numerous molecular methods for spinal muscular atrophy (SMA) detection have been exploited, most of them are laborious, time consuming and costly. Recently, gold nanoparticles (AuNPs) have attracted attention in the field of colourimetric bioanalysis, because AuNP aggregation can be tracked with the naked eye as well as ultraviolet–visible (UV–vis) peak analysis. Here, based on a non-cross linking platform, a colourimetric-based method was used to evaluate the capability of thiolated oligo-AuNPs (Au nanoprobes) to distinguish between normal individuals, carriers and those with SMA. In this platform, removal of the repulsive force of the Au nanoprobes using high salt concentration solutions forced them to aggregate. Amplified DNA products from 20 blood samples were hybridised with the Au nanoprobes. UV–vis spectra and peak analysis ratios of SMA-positive samples revealed that, following salt addition, the unhybridised Au nanoprobes progressively aggregated and their absorption peak shifted to longer wavelengths ($P < 0.05$), observed as a colour change from red to violet-purple. In contrast, colourimetric discrimination between normal and carrier samples following salt addition was not possible because of the small differences in their spectra and aggregation indices. Using this method, patients can be screened in <30 min.

1 Introduction

One of the most prominent autosomal-recessive genetic abnormalities is spinal muscular atrophy (SMA) [1]. This fatal disorder is characterised by the lack or malfunction of the survival of motor neuron (SMN) protein. SMN proteins are encoded by the *SMN* genes, *SMN1* and *SMN2*, located on chromosome 5q13 [2]. These genes differ by five nucleotide base pairs (one in *exon 7*, *exon 8*, and *intron 6*; and two in *intron 7*). A crucial transition (C → T) in *exon 7* of *SMN2* compared with *SMN1* produces non-carboxyl-terminal proteins that cannot oligomerise. Hence, these non-functional SMN2 proteins cannot effectively form stable ribonucleoprotein complexes that consequently cannot function normally in neuromuscular growth and maturation [3]. Normal individuals are homozygous for *SMN1* and *SMN2* genes, but the carrier and affected cases are heterozygous and homozygous for *SMN1* deletion, respectively. In 94% of patients who have a homozygous deletion of *SMN1*, the motor neurons degenerate and the disease leads to progressive paralysis or death.

Owing to the severity and frequency of SMA and the high number of carriers (1/10 000 and 1/50, respectively), various molecular techniques have been developed for its detection, including polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) [4], allele-specific PCR [5], multiplex ligation dependent probe amplification [6], matrix-assisted laser desorption ionisation-time of flight mass spectrometry [7], denaturing high-performance liquid chromatography [8], fibre-optic biosensor [9], real-time PCR [10] and capillary electrophoresis [11]. However, few clinical laboratories carry out these tests because of the cost, time and complexity of the assays. Therefore, development of a cheap, rapid and simple method is necessary.